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Pitfalls in the Nutritional Management of Very Low Birth Weight Infants: Lessons to be learned from Detailed Chart Analyses

Iris Alexa Howaldt[1], Stephan Seeliger[2] and Helmut Küster[1]*

[1]Clinic for Paediatric Cardiology, Intensive Care and Neonatology, University Medical Centre, Georg-August-Universität Göttingen, Germany

[2]Clinic for Paediatrics, St. Elisabeth Hospital, Neuburg an der Donau, Germany

Abstract

Background: Normal long-term neurodevelopmental outcome of very low birth weight infants requires adequate nutrition. The latter depends on a precise nutritional protocol and regular checks of adherence to its content. The scope of this study was to reveal factors with potential negative influence on adequate nutritional support of very low birth weight infants in a level IV neonatal intensive care unit.

Methods: A detailed chart analysis investigated the adherence to the local protocol for enteral and parenteral nutrition and the resulting growth of very low birth weight infants stratified by predefined criteria in four 250 g strata.

Results: The median [IQR] birth weight was 1065 (439) g, gestational age was 29.1 (3.4) weeks. Weight gain was 14.8 g/kg/d, which was equivalent to the lower range of intrauterine growth. Hence, z-score of 0.59 at birth dropped to -1.39 at discharge. Chart analysis revealed six reasons for inadequate growth: 1) Delayed postnatal start of parenteral protein and fat supplementation on day two; 2) Slower than intended advancement of oral feeds by in median 7.8 instead of the proposed 20 mL/kg/d; 3) Failure of using the most current body weight for calculation; 4) Inadequate total protein intake: 7.3 g/kg/d cumulative protein deficit already on day 8, the intended 4 g/kg/d of protein were not reached on 59% of all hospital days; 5) Reduction of milk supplementation ahead of schedule; 6) Interruption of parenteral nutrition during infusion of antibiotics.

Conclusion: To achieve optimal quality of care regular reviews of adherence to internal guidelines are essential. Certain errors in management may only be detected by regular independent detailed analysis of charts and daily practice.

Keywords: Nutrition; Very low birth weight infant; Newborn; Neonatal intensive care; Health and safety; Quality of health care

Abbreviations: BPD: Bronchopulmonary Dysplasia; DOL: Day of Life; IQR: Interquartile Range; IVH: Intraventricular Haemorrhage; NEC: Necrotizing Enterocolitis; PDA: Patent Ductus Arteriosus; PVL: Periventricular Leucomalacia; ROP: Retinopathy of Prematurity; SGA: Small for Gestational Age

Introduction

Nutrition and growth are important in neonatal care. Especially for Very Low Birth Weight (VLBW) infant's adequate growth has a high impact on long term outcome: Early protein intake, postnatal growth and particularly gain in head circumference corresponding to intrauterine reference curves are associated with good neurocognitive development [1-4]. Several studies have documented that inadequate nutritional intake may lead to extra-uterine growth retardation [5-7] which to a large extent may be a result of cumulative deficits in caloric and protein intake starting in the first week of life [6-8]. This postnatal malnutrition is in part due to a slow increase of enteral feeding assuming intolerance of the gut with increased risk of Necrotizing Enterocolitis (NEC). These reasons have been disproven by several studies: An increase of oral feedings by up to 35 mL/kg per day did not result in a higher incidence of NEC [9,10]. In addition, high intake of amino acids of 3.5 g/kg per day from Day of Life (DOL) 1 was well tolerated in preterm infants [11].

In order to achieve optimal growth in VLBW infant's nutritional support should be started immediately after birth [12]. Especially a positive nitrogen balance should be achieved as soon as possible and constantly maintained thereafter. For this purpose, a protocol for parenteral and enteral nutrition is required [9].

Our nutritional protocol for neonates was redone in 2009 based on recommendations by ESPGHAN in 2005 [13]. This protocol has been used since without any evaluation concerning the adherence to its content or its effects. Therefore, in this study we assessed (1) The current practice in our NICU regarding parenteral and enteral nutrition, (2) The adherence to our protocol and (3) Weight and head circumference gain during the entire hospital stay in a stratified sample of our VLBW infants.

Methods

Patients

Eligible were inborns with a birth weight of 500-1499 g treated in our level IIIB intensive care unit. In order to be treated by a constant feeding regimen infants had to be born from January 2010 and discharged home not later than June 2011 (n=56). Exclusion criteria were multiples (n=17) as well as those with severe malformations (n=3), operations involving the gastrointestinal tract (n=1) or NEC grade II or III (n=3) of these eligible 32 infants 20 were selected for detailed chart analysis to have four equally sized 250 g strata of birth weight (500-749 g, 750-999 g, 1000-1249 g, 1250-1499 g) with equal distribution of

***Corresponding author:** Küster H, Clinic for Paediatric Cardiology, Intensive Care and Neonatology, University Medical Centre, Georg-August-Universität Göttinge, E-mail: helmut.kuester@med.uni-goettingen.de

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gender. The limited number of patients with a birth weight of 500-749 g restricted the stratum size to five infants.

This study was approved by the local ethical committee of the University Medicine Göttingen (DOK_44_2012).

Data collection

For retrospective analysis, we extracted all parameters with any relevance to nutrition from our paper charts from admission until discharge from our hospital. Because body weight was measured every second day only, daily values for weight were determined by linear interpolation. The value for head circumference on day 14 was calculated in a similar manner if no value was documented on that specific day. According to the routine clinical practice of written documentation, all parameters were collected in 24 hourly intervals of 6 pm to 6 pm. If patients were born before 6 pm fluids given continuously during this incomplete first day were projected onto 24 hours assuming that the child would have received this calculated amount if born at 6 pm. In contrast, fluid boluses were included into our calculation as given.

Nutritional regimen

The protocol used during the study period was based on 2005 ESPGHAN guidelines12 and specified the following:

Parenteral nutrition was to be started on day one with 80 mL/kg/d and increased daily up to 150 mL/kg/d on day 5. Amino acids were to be advanced from 1.5 g/kg/d on day one to 4 g/kg/d on day three. Fat was to be started with 0.5 g/kg/d on day one in infants with a birth weight >800 g, on day three for those <800 g and increased by 0.5 g/kg per day until 3 g/kg/d, to be infused over 20 hours. Carbohydrates were to be started between 6-11 g/kg/d and increased up to 18 g/kg/d according to blood glucose levels.

Enteral nutrition by bolus feeding was to be started on day one with 0.5 mL/kg of glucose 5%, followed from day two by breast milk as soon as available or preterm formula. Oral feeds were to be increased by 20 mL/kg/d until full feeds were achieved. Fortifier (FM 85, Nestlé, Frankfurt/Main, Germany; Duocal, Nutricia GmbH, Erlangen, Germany) was to be added to breast milk after day 10 of life when a 5 mL-single bolus feed was tolerated and slowly increased to 5%. Until April 2010 preterm infant formula was fortified with Duocal and breast milk with FM 85. After this date FM 85 was used only. Gastric residuals were to be returned if the pH was acidic and complemented to full feeds. Bloody or bilious residuals were to be discarded.

For daily calculation of nutrition, a Microsoft Excel 2007 spreadsheet (Microsoft, Redmond, USA) was used that gave details for the individual nutritional components given.

Statistics

For each patient, continuous data were summarized using means. Each strata or the whole group was described by median and interquartile range to account for the limited number of patients. Trends were computed by calculating a mean for each infant and then a median of all means. Categorial data are expressed as frequency and percentage.

To calculate calories, 4.1 kcal/g were used for carbohydrates and amino acids, 9.3 kcal/g for fat. To account for their reduced resorption in the intestine, calories for orally provided amino acids and fat were included by 75%. This number takes into consideration an intestinal utilization rate of 50% on average for the different amino acids plus a 25% delayed release into the systemic circulation [14]. For fat, an intestinal non-resorption rate of 10%-40% has been described [15]. If both breast and formula milk were given on the same day but their relative amounts not exactly documented, equal amounts were assumed.

Body weight and head circumference were converted into z-scores using the best fitting database published for German newborn infants [16].

To analyse the effect of group membership (study group vs. not analysed) a Wilcoxon test was used for (non)-continuous data and a Chi-squared test for dichotome endpoints using STATISTICA 10 (StatSoft, Hamburg, Germany). The level of significance was set to α=0.05. All remaining calculations were performed using Microsoft Excel 2007 (Microsoft, Redmond, USA).

Results

The twenty patients selected for analysis had a median birth weight of 1065 g and a median gestational age of 29 weeks. Except for the gender distribution, these 20 patients did not differ in their demographical data from those 12 patients who also fulfilled our study criteria but were not included in the analysis (Table 1). After one week of life, the infants had achieved in median (interquartile range; IQR) 140 mL/kg per day (18) in parenteral plus enteral fluid intake and had regained their birth weight. After 11.5 days, they obtained 120 mL/kg per day in oral feeds and after 19.5 days 150 mL/kg per day (Table 2). Parenteral nutrition was discontinued when 140 mL/kg per day oral were reached which was on DOL 20 and 9 for stratum I and IV, respectively. In average patients remained 10 mL/kg per day below the intended fluid supply specified in our guideline (data not shown). Caloric intake was 120 kcal/kg (oral plus parenteral) on day 10. From that day on the weight gain was 14.8 g/kg per day which was less than intrauterine growth (Figure 1). Birth weight plus 20% was reached on DOL 20 with little variation between the four strata. Towards the end of the hospital stay the growth curves in all four strata deviated more than before from intrauterine curves, especially those of the lightest infants (stratum I).

Infants' weights started at a median z-score of -0.59 at birth for all groups. The initial weight loss resulted in a drop of weight to a z-score of -0.94 on DOL 14. Except for stratum IV, z-score dropped further during the hospital stay by an additional 0.5 (Table 3).

For calculation of weight and head circumference at discharge that of the third infant of each stratum is shown in Table 3.

In order to understand underlying causes of the decline in z-score we compared median values for total caloric and protein intake to recommended intakes. While our guideline aimed for a total protein intake of 4 g/kg/d on day 3 of life, it took 8 days to achieve this value in our study group. This resulted in a protein deficit of 7.3 g/kg/d on DOL 8. The deficit continuously increased to between 57 and 22 g/kg/d at discharge for stratum I and IV, respectively (Figure 2). The study group remained below the protein intake aimed for on 59% of their hospital days. Not receiving the recommended protein intake was seen in all four strata with no correlation to birth weight.

In a quarter of the infants, the body weight used for calculation of nutrition was two days old and resulted in a reduced nutritional input for the actual weight. Until DOL 28 the percentage of infants in whom the most recent body weight was used for calculation of intake increased to 58%.

After transfer from intensive to intermediate care supplementation of human milk and preterm formula was not increased to fit to the

		All eligible patients	Patients not analysed	Study Group	p
Number	n	32	12	20	
Gestational age	weeks	29.3 (3.7)	29.3 (5.6)	29.1 (3.4)	0.33
Birth weight	g	1090 (409)	1120 (440)	1065 (439)	0.23
SGA (<10. percentile)	n (%)	6 (19)	1 (8)	5 (25)	0.15
Head circumference at birth	cm	26 (3.1)	26.7 (3)	25.9 (3.6)	0.22
Gender (female : male)	n	22:10	11:1	11:9	**0.03**
IVH °3 + 4	n (%)	2 (6)	1 (8)	1 (5)	0.71
PVL	n (%)	0 (0)	0 (0)	0 (0)	-
BPD	n (%)	3 (9)	1 (8)	2 (10)	0.88
ROP °3-5[1]	n (%)	2 (6)	0 (0)	2 (10)	0.26
PDA medical treatment	n (%)	11 (34)	4 (33)	7 (35)	0.92
PDA surgery	n (%)	7 (22)	4 (33)	4 (20)	0.4
Sepsis	n (%)	15 (47)	5 (42)	10 (50)	0.65
Operation[2]	n (%)	10 (31)	5 (42)	5 (25)	0.32

Note: Data are reported as median and (interquartile range). [1]ROP °3 only, [2]Two because of ROP. P values were calculated between 'Patients not analysed' and 'Study group'.

Table 1: Characteristics of the study group and all eligible infants.

		All	Stratum I 500-749 g	Stratum II 750–999 g	Stratum III 1000–1249 g	Stratum IV 1250–1499 g
120 kcal/kg/d	(DOL)	10 (7.3)	11 (1)	13 (5)	8 (6)	5 (3)
120 mL/kg/d oral	(DOL)	11.5 (8.3)	16 (5)	11 (6)	9 (5)	8 (3)
End of parenteral nutrition[1]	(DOL)	13 (10)	20 (17)	14 (8.8)	9 (6)	9 (17)
4g/kg/d total protein achieved first[2]	(DOL)	8 (10)	14 (36)	8 (3)	7 (5)	6 (3)
Days with / without 4g/kg/d total protein	(days / days)	20 / 38	33 / 85	24 / 41	14 / 24	23 / 17
Regained birth weight	(DOL)	8 (6.3)	1 (9)	10 (5)	7 (1)	8 (4)
Weight gain after DOL 10	(g/kg*day)	15 (3.7)	15 (3.2)	15 (1.4)	16 (7.2)	14 (3.2)
Birth weight +20%	(DOL)	20 (6)	20 (1)	22 (2)	20 (7)	17 (4)
1500 g achieved	(DOL)	28 (31.5)	62 (13)	37 (2)	23 (7)	12 (4)
Gestational age at discharge	(weeks)	38.5 (2.9)	39.8 (0.9)	38.8 (1.4)	37.6 (2.9)	36.5 (2)
Weight at discharge	(g)	2478 (620)	2808 (95)	2560 (820)	2395 (680)	2345 (120)
Head circumference at discharge	(cm)	32.7 (1.7)	32.8 (1.5)	33 (1.3)	31.7 (0.8)	33.2 (0.5)
Hospital stay	(days)	64 (47)	107 (15)	65 (17)	49 (47)	40 (14)

Note: Values are reported as median and (interquartile range). [1]First day without parenteral nutrition, [2]Given is the DOL when infants received 4 g/kg/d total proteins on three consecutive days. For those two infants who never reached this amount during their hospital stay the day after discharge was used for calculation.

Table 2: Main outcome data of the study group.

	Weight			Head circumference		
	At birth	On DOL 14	At discharge	At birth	On DOL 14	At discharge
All	-0.59	-0.94	-1.50	-0.60	-1.29	-1.54
Stratum I	-0.65	-0.96	-1.57	-1.17	-1.50	-1.92
Stratum II	-0.23	-0.94	-1.45	-0.58	-1.33	-1.00
Stratum III	-0.54	-0.92	-1.43	-0.25	-1.25	-2.00
Stratum IV	-0.43	-0.94	-1.18	0.00	-0.95	-0.77

Note: For calculation of weight and head circumference at discharge that of the third infant of each stratum is shown.

Table 3: Median z-scores for weight and head circumference of each stratum.

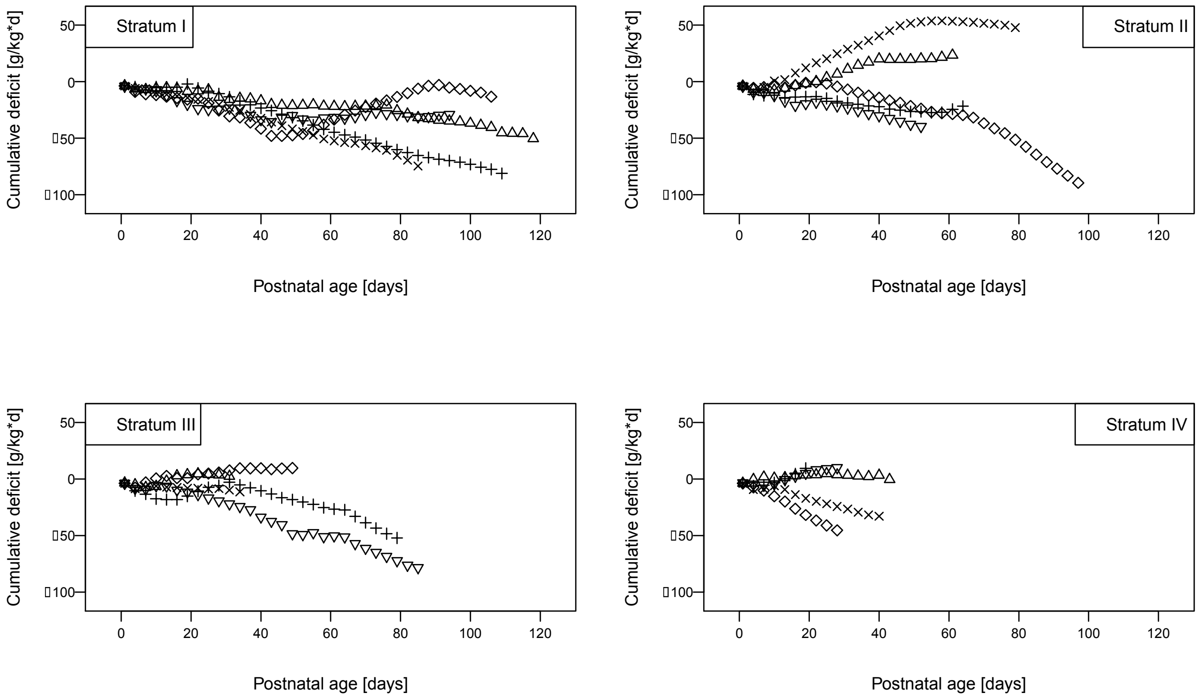

Figure 1: Weight gain from birth until discharge for each stratum.

Note: Shown is body weight against postnatal age until discharge home separately for each stratum (dots). Solid lines represent the reference weight curves for the corresponding stratum as calculated from German data [16].

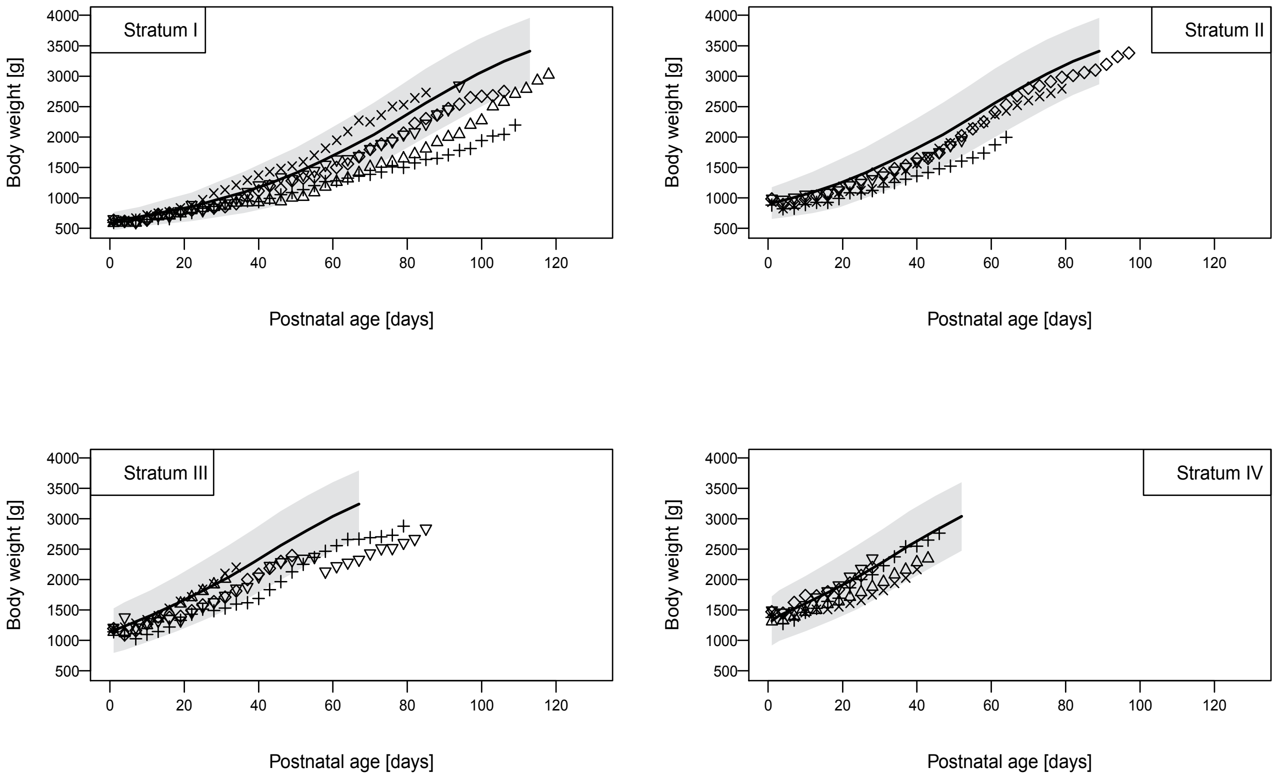

Figure 2: Protein deficit during the hospital stay.

Note: Shown are the cumulative protein deficits during the hospital stay for all four strata: every patient is shown as dotted line.

current body weight in a quarter of the infants. In preparation for discharge, supplementation was reduced in 9 infants in median eight days prior to discharge and stopped completely in another 5 infants 12 days before the day of discharge.

Discussion

Numerous studies have shown inadequate postnatal weight gain in VLBW infants when compared to intrauterine growth curves with [5–7]. This growth failure is associated with adverse neurocognitive development [1-4]. As shown in other studies, analysis of a cohort of our VLBW infants revealed an insufficient weight gain when compared to reference curves for intrauterine growth. Speculations for underlying reasons are plenty but supporting data are scarce. Analysis is frequently based on the scheduled intake according to a study protocol or on data extracted on a few specific days of life. Using intakes actually achieved as analyzed on a day-by-day basis is not common. We therefore analyzed a stratified cohort of VLBW infants in regard to our current nutritional practice towards oral and parenteral intake by each individual component and the resulting growth of these infants.

Already at birth, the study group had a negative z-score because 20% of the infants were born as SGA. This overrepresentation of SGA infants is most likely because a pregnancy is often terminated because of intrauterine growth failure as can be seen in most birth cohorts. After the initial drop of weight seen in every newborn, the infants' growth started earlier than reported by other groups [17-22]. This could be a result of our infants receiving a total caloric intake of 100 kcal/d on DOL 6 7 compared to DOL 10 and DOL 16 as reported by Diekmann, et al. and Aktintorin, et al. respectively [18,19]. This is in spite of the fact that our calculation included only 75% of the oral calories from amino acids or fat because of their reduced enteral absorption. Our high caloric input resulted in only 13 versus 30 days in other studies with a similar population to achieve full enteral feeds [17]. In spite of this early high caloric intake, the infants' weight gain during the remaining hospital stay was at a similar rate compared to published data and at the lower end of the range recommended [17-19, 21-24]. This was unexpected as our nutrition guideline was written according to recommendations by ESPGHAN [13]. Our detailed analysis revealed six potential reasons:

Start of parenteral nutrition

Our guideline postulated to give 1.5 g/kg of protein on the first DOL, 3 and 4 g/kg on day 2 and 3, respectively. However, according to our chart analysis, the infants had no amino acids on the first DOL. This was because all infants received on admission a standard infusion solution ready for instant use that did not contain amino acids. In addition, on day 2 and 3 they received only 2.2 g/kg and 3.4 g/kg, respectively. Stratum I even needed two weeks to receive 4 g/kg/d of protein in median, which is more than four times longer than aimed for. This reduced protein intake has a significant impact. Studies have demonstrated that an amino acid supply of at least 4 g/kg/d is essential for adequate growth [13,15,23].

Increase of oral nutrition

Full oral feeds of 150 mL/kg were achieved on day 20, which is equivalent to a median daily increase for all infants of 7.8 mL/kg/d. This is substantially below the intended 20 mL/kg/d. According to the charts, the underlying reasons for this slow advancement of oral feeds were gastric residuals or the infants' clinical appearance like abdominal distension. Studies have shown that a daily increase of up to 35 mL/kg per day can be achieved without a higher incidence of NEC in infants weighing between 501 g and 1500 g at birth [9]. In this study, the "fast" group reached 160 mL/kg orally per day after 11 days in spite of the fact that oral feeds were started only on day 4. These 7 days needed to achieve full oral feeds are in agreement with our guideline but are contrasted by the result of our analysis. The influence of gastric residuals on oral feedings as found in our analysis is not supported by a study from Mihatsch, et al. [24]. He tested a feeding regimen in clinically stable extremely low birth weight infants <1000 g and showed that gastric residuals of up to 2 mL/3 mL in infants ≤750 g/>750 g as well as their colour have no impact on the establishment of enteral feeding. Miller, et al. described in their retrospective chart review the transitional phase from parenteral to enteral nutrition as the time with the highest incidence of poor growth due to insufficient protein supply [25]. This phenomenon was not observed in our population where growth retardation was seen later during the hospital stay.

Incorrect calculation of nutrition

Chart analysis showed that in 42% of intensive care days an older than the most recent body weight was used for calculation of oral and parenteral nutrition. As a result, infants received in average 10 mL/kg/d fluids less than recommended by the local guideline for the entire hospital stay. Not using the most recent weight for calculation might also be the reason that in our study group parenteral nutrition ended when only 140 mL/kg/d oral feeds was reached. While a reduction of fluid intake to 140 mL/kg/d or even less might have been done intentionally in those infants with PDA or BPD, especially when on diuretics, this reasoning was neither true for most of the infants nor was it compensated by an appropriate increase in calories. An additional reason may be that gastric residuals were discarded without compensational parenteral nutrition.

Inadequate total protein intake

Protein given beyond the first days of life was below our local guideline, which resulted in an accumulation of protein deficit over a long time period. The total protein intake remained below 4 g/kg/d on 59% of the hospital days for all infants and 80% for stratum I only. It has to be kept in mind that for oral proteins (and lipids) only 75% were considered to be absorbed in the gastrointestinal tract and therefore included in these calculations [14,15]. This might not have been taken into account when these infants were cared for.

End of milk supplementation

Reduction or termination of fortification of human milk or formula towards the end of the hospital stay was often observed. This was in parallel with a further deviation of growth from the intrauterine curve in some infants. The infants' transfer from intensive to intermediate care sometimes triggered such a change in fortification or to a formula with lower caloric density. At this time, these infants were still partially tube fed and therefore not able to compensate decreased caloric density by increased volume. In addition, the social and financial background of some families made it reasonable to change from preterm to term formula and to end fortification to ensure an easier handling during the time after discharge from hospital.

Antibiotics for nutrition

Of major influence to the caloric intake was a general concept of the nurses that the total amount of fluid should be kept constant at the set rate with highest priority. This led to a reduction in parenteral nutrition whenever intravenous antibiotics or other intravenous medications were given. Consequently, the desired drug diluted in 10% glucose was frequently infused for one hour instead of a high caloric parenteral nutrition with amino acids. In an infant receiving several different antibiotics several times a day this concept resulted in a reduction of parenteral nutrition infused to only 2/3 of that intended. This problem was further aggravated by the fact mentioned above that the total amount of fluid actually achieved was in median only 140 instead of the intended 150 mL/kg/d.

Implications

Having defined guidelines for patient care has been shown to by itself result in an improvement of the quality of care. However, the existence of such guidelines does not guarantee that their content is translated into daily routine as shown by our analysis. Six quality problems were found where nurses and physicians did not follow the existing guideline. Some of these could be detected easily; other fundamental mistakes in management could be uncovered only by very detailed analysis of procedures and habits.

To avoid prescription errors, software used for daily calculation of nutrition should have a user friendly and well-arranged data entry surface. The most relevant fields for data entry and calculated data should be highlighted. Colour coded plausibility checks should help to insure correct data entry as well as adherence to desired values. In addition, the software should show trends in the nutritional regimen and the resulting growth by easy to use analysis tools. Each of these measures would result in more consistent and user-independent patient care. Furthermore, close cooperation with a nutritional specialist and a pharmacist may help to improve individualised protocols for nutrition. In addition, each item documented in patient care, regardless of being electronically or on paper, should be specified in detail and reviewed regularly. Some of these aspects have been postulated before [26] and are now supported by our data.

As a consequence, our nutritional regimen was improved by revising the software used for daily calculation of enteral and parenteral nutrition. In addition, a team of doctors, nurses and pharmacists will review the translation of our local guideline into clinical practice on a regular basis.

Limitations of the study

This study included only a small sample size. However, this group of patients was analysed in detail and a large number of data points extracted from each patients' chart. This resulted in 734 (961) data points per infant (median (IQR)). Such an approach of a detailed analysis of a limited number of patients was preferred in order to have results from a stratified group of patients who were raised during a period with a uniform nutritional regimen. The exclusion of multiples and patients with gastrointestinal problems may influence mean values and in the limited number of infants preponderate the results obtained.

A restriction to a small but homogeneous study group of four equally sized strata of well-defined patients and the collection of a large pool of clinical and nutritional data during the whole hospital stay partially should have compensated for these limitations.

Conclusion

Certain fundamental shortcomings in the management of preterm infants may only be detected by independent detailed analysis of charts and habits. Electronic tools and documentation of patient care should have detailed definitions and designed to avoid errors. To achieve optimal quality of care regular reviews of internal guidelines are essential and should include defined cornerstones of care.

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Conflicts of Interest

None to declare.

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